DETAILED ACTION

Reasons for Allowance

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Norma Henderson (Reg. No. 39,219) on August 27, 2010.

2. The application has been amended as follows:

Cancel claims 15, 23, 25, 28, and 30 and combine claim 24 with claims 11-14, 16, 19-22, 26, 27, and 29.

11. (Currently Amended) A method for removing or controlling errors in a plurality or pool of nucleic acid molecules [comprising a user-specified sequence composition and length], the method comprising:

a) [providing a] synthesizing said plurality or pool of nucleic acid molecules[, the nucleic acid molecules being intended to have the user-specified sequence composition and length and being synthesized] by the steps of:

providing a first immobilized nucleic acid comprising a first 5' region and a first 3' region;

providing [at least] a second immobilized nucleic acid comprising a second 5' region and a second 3' region, wherein said second 3' region and said first 5' region comprise identical nucleic acid sequences;

[contacting] hybridizing said first immobilized nucleic acid with an oligonucleotide under conditions promoting hybridization of said oligonucleotide to said first 3' region, extending [and extension of said] the hybridized oligonucleotide, and producing [to produce] a first extension product comprising a [first extension product] 3' region that is complementary to said first 5' region; and

[contacting] hybridizing said second immobilized nucleic acid with said first extension product under conditions promoting hybridization of said 3' region of said first extension product [3' region] to said second 3' region, extending [and extension of said] the 3' region [hybridized] of said first extension product [3' region], and producing [to produce] a second extension product comprising a [second extension product] 3' region that is complementary to said second 5' region, wherein said second extension product comprises a sequence [said] complementary to said first 3' and 5' regions and said second 3' and 5' regions, and [said nucleic acid molecule comprises] the individual nucleic acid molecules of said second extension product comprise said plurality or pool of nucleic acid molecules;

b) distinguishing between error-free and error-containing nucleic acid molecules within said plurality or pool of nucleic acid molecules[, wherein the error-free nucleic acid molecules are synthesized nucleic molecules that have the user-specified sequence composition and length and the error-containing nucleic acid molecules are synthesized nucleic molecules that do not have the user-specified sequence composition and length]; and

c) selectively amplifying only the error-free nucleic acid molecules from said plurality or pool of nucleic acid molecules, thereby decreasing the relative amount of the error-containing nucleic acid molecules within said plurality or pool of nucleic acid molecules.

12. (Currently Amended) A method for removing or controlling errors in a plurality or pool of nucleic acid molecules [comprising a user-specified sequence composition and length], the method comprising:

a) [providing a] synthesizing said plurality or pool of nucleic acid molecules[, the nucleic acid molecules being intended synthesized to have the user-specified sequence composition and length and being synthesized] by the steps of:

providing a first immobilized nucleic acid comprising a first 5' region and a first 3' region;

providing [at least] a second immobilized nucleic acid comprising a second 5' region and a second 3' region, wherein said second 3' region and said first 5' region comprise identical nucleic acid sequences;

[contacting] hybridizing said first immobilized nucleic acid with an oligonucleotide under conditions promoting hybridization of said oligonucleotide to said first 3' region, extending [and extension of said] the hybridized oligonucleotide, and producing [to produce] a first extension product comprising a [first extension product] 3' region that is complementary to said first 5' region; and

[contacting] hybridizing said second immobilized nucleic acid with said first extension product under conditions promoting hybridization of said 3' region of said first extension product [3' region] to said second 3' region, extending [and extension of said] the 3' region [hybridized] of said first extension product [3' region], and producing [to produce] a second extension product comprising a [second extension product] 3' region that is complementary to said second 5' region, wherein said second extension product comprises a sequence [said]

complementary to said first 3' and 5' regions and said second 3' and 5' regions, and [said nucleic acid molecule comprises] the individual nucleic acid molecules of said second extension product comprise said plurality or pool of nucleic acid molecules;

b) distinguishing between error-free and error-containing nucleic acid molecules within said plurality or pool of nucleic acid molecules[, wherein the error-free nucleic acid molecules are synthesized nucleic molecules that have the user-specified sequence composition and length and the error-containing nucleic acid molecules are synthesized nucleic molecules that do not have the user-specified sequence composition and length]; and

c) correcting errors in said plurality or pool of nucleic acid molecules by using the error-free nucleic acid molecules in said plurality or pool of nucleic acid molecules as [a] templates for [repair of] repairing said error-containing nucleic acid molecules.

13. (Currently Amended) A method for removing or controlling errors in a plurality or pool of nucleic acid molecules [comprising a user-specified sequence composition and length], the method comprising:

a) [providing a] synthesizing said plurality or pool of nucleic acid molecules[, the nucleic acid molecules being intended to have the user-specified sequence composition and length and being synthesized] by the steps of:

providing a first immobilized nucleic acid comprising a first 5' region and a first 3' region;

providing [at least] a second immobilized nucleic acid comprising a second 5' region and a second 3' region, wherein said second 3' region and said first 5' region comprise identical nucleic acid sequences;

[contacting] hybridizing said first immobilized nucleic acid with an oligonucleotide under conditions promoting hybridization of said oligonucleotide to said first 3' region, extending [and extension of said] the hybridized oligonucleotide, and producing [to produce] a first extension product comprising a [first extension product] 3' region that is complementary to said first 5' region; and

[contacting] hybridizing said second immobilized nucleic acid with said first extension product under conditions promoting hybridization of said 3' region of said first extension product [3' region] to said second 3' region, extending [and extension of said] the 3' region [hybridized] of said first extension product [3' region], and producing [to produce] a second extension product comprising a [second extension product] 3' region that is complementary to said second 5' region, wherein said second extension product comprises a sequence [said] complementary to said first 3' and 5' regions and said second 3' and 5' regions, and [said nucleic acid molecule comprises] the individual nucleic acid molecules of said second extension product comprise said plurality or pool of nucleic acid molecules;

b) identifying error-containing nucleic acid molecules [of] within said plurality or pool of nucleic acid molecules[, wherein the error-free nucleic acid molecules are synthesized nucleic molecules that have the user-specified sequence composition and length and the error-containing nucleic acid molecules are synthesized nucleic molecules that do not have the user-specified sequence composition and length]; and

c) removing the error-containing portions of said error-containing nucleic acid molecules [to produce], thereby producing error-free nucleic acid molecules and removing or controlling errors in said plurality or pool of nucleic acid molecules [sequences; and

d) combining said error-free nucleic acid sequences to yield error-free nucleic acid molecules].

14. (Currently Amended) The method of claim 11, the [step of] selectively amplifying step further [comprising] comprises the step of [combining at least one] contacting said error-containing nucleic acid molecules from said plurality or pool of nucleic acid molecules with at least one component that prevents amplification of [the] said error-containing nucleic acid molecules, wherein the errors in said error-containing nucleic acid molecules are mismatches and the component is a mismatch binding protein that binds selectively to DNA duplexes containing mismatches.

16. (Currently Amended) The method of claim 14, wherein the component is cross-linked to [the] said error-containing nucleic acid molecules.

20. (Currently Amended) The method of claim 12, the step of correcting errors further comprises [comprising] the step of producing nucleic acid strands that are selectively hemi-methylated [targeting errors] via methylation and [selective] site-specific demethylation.

21. (Currently Amended) The method of claim 12, wherein the errors in the error-containing nucleic acid molecules are mismatches, the step of correcting errors [comprising] further comprises the steps of:

[mismatch recognition on said error-containing nucleic acid molecules to] identifying the errors in specific bases [errors] in said error-containing nucleic acid molecules by binding the mismatched bases of said error-containing nucleic acid molecules with a mismatch binding protein that binds selectively to DNA duplexes containing mismatches;

[cleavage of] cleaving the mismatched bases of said error-containing nucleic acid molecules [said specific base errors]; and

[replacement of said] replacing the cleaved bases [errors] with [the] correct bases [according to] based on the nucleotide sequences of the templates.

22. (Currently Amended) The method of claim 21, wherein the [steps of mismatch recognition and cleavage are] cleaving step is performed by [a resolvase,] a single-stranded nuclease[,] or [a combination of a mismatch binding protein and] a nuclease.

24. (Currently Amended) The method of claim [12, the step of correcting errors comprising the step of generating at least one repair template by] 21, wherein said replacing step is performed by strand invasion and branch migration.

26. (Currently Amended) The method of claim 13, wherein the errors in the error-containing nucleic acid molecules are mismatches, the [step of] identifying and removing [errors comprising] steps further comprise the steps of:

[mismatch recognition on said error-containing nucleic acid molecules to] identifying the errors in specific bases [errors] in said error-containing nucleic acid molecules by binding the mismatched bases of said error-containing nucleic acid molecules with a mismatch binding protein that binds selectively to DNA duplexes containing mismatches; and

[cleavage of] cleaving the mismatched bases of said error-containing nucleic acid molecules [said specific base errors].

27. (Currently Amended) The method of claim 26, wherein the [steps of mismatch recognition and cleavage are] cleaving step is performed by [a resolvase,] a single-stranded nuclease[,] or [a combination of a mismatch binding protein and] a nuclease.

29. (Currently Amended) The method of claim 13, wherein the errors in the error-containing nucleic acid molecules are mismatches and the [step of] removing step [errors] is performed [by] using a mismatch binding protein to identify the errors in specific bases [sequence errors] in said error-containing nucleic acid molecules and a nuclease to cleave the mismatched bases in said specific bases of said error-containing nucleic acid molecules [sequence errors].

3. The following is an examiner's statement of reasons for allowance:

Claims 11-14, 16, 19-22, 24, 26, 27, and 29 are allowable in light of applicant's amendment filed on May 19, 2010 and the examiner's amendment. The rejections under 35 U.S.C. 112, first and second paragraphs have been withdrawn in view of applicant's amendment filed on May 19, 2010 and the examiner's amendment. The closest prior arts in the record are Wagner, Jr. (US Patent No. 6,114,115, published on September 5, 2000) and Modrich *et al.,* (US Patent No. 5,922,539, published on July 13, 1999). These prior arts do not teach or suggest step a) of independent claims 11-13. These prior arts either alone or in combination with the other art in the record do not teach or reasonably suggest a method for removing or controlling errors in a plurality or pool of nucleic acid molecules which comprises all limitations recited in claims 11-13.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
August 27, 2010